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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,064	08/02/2005	Pierre Michel Desmons	LEXSA.P48	4877

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,064	DESMONS ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) *23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-22,26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and remarks, filed 12/8/2009, are acknowledged. Claims 1-16 are cancelled. New claims 17-29 are added. Claims 17-29 are pending.

Election/Restrictions

Newly submitted claims 23-25 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons:

Claims 23 and 25 are part of Group V and claim 24 is part of Group VI as set forth in the restriction requirement mailed on 1/9/2006.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 23-25 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 17-22 and 26-29 are currently under examination.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is noted that applicant's arguments are directed toward the rejection over Berthet, Vermont, and Baker. However, applicant then mentions Vermont, Baker, and Granoff. There are two rejections under 35 USC 103(a), one over Berthet, Vermont, and Baker and one over Granoff, Vermont, and Baker. As it appears that the same arguments apply to both rejections, the examiner will treat the arguments as if both rejections are being argued.

Claims 17-19, 26, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) in view of Vermont *et al.* (Infect. Immun., 70:584-590, 2/2002) and Baker *et al.* (J. Paediatr. Child Health, 37:S13-S19, 2001), for the reasons set forth in the rejection of 1, 6-7, and 16 in the previous office action.

Applicant argues:

1. That the prior art does not disclose or suggest the combination and proportions recited by the claims.

2. That the claimed combination provides unexpected results, namely, "immunogenicity against heterologous strains" and being "free of immune interference." Applicant argues that combining diverse blebs is discouraged in the prior art because of possible immune interference.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, the combination of prior art references provides a composition containing bleb composition comprising blebs from CU-385 and blebs from strain B:4:P1.7b,4. The specification indicates (and applicant has previously agreed, see remarks filed 11/9/2007) that these strains have the appropriate amounts of PorA. There does not need to be any recognition in the prior art that these strains have the claimed percentages because the fact is that the strains *do* have those claimed percentages.

Regarding argument 2, applicant has not provided any evidence of unexpected results. Applicant has not provided any evidence that the strains would not have separately been immunogenic against heterologous strains and, contrary to applicant's assertion, the art specifically discloses combinations of blebs. Therefore, one would not expect immune interference to be an issue.

As outlined previously, the instant claims are drawn to a multivalent bleb composition comprising a first bleb composition comprising a first bleb preparation deficient in PorA, and a second bleb preparation that is not deficient in PorA.

Berthet *et al.* disclose a multivalent vaccine comprising mixtures of meningococcus bleb preparations as well as a pharmaceutically acceptable excipient (see page 36, lines 5-28 and page 33, lines 1-5). Said vaccine comprises mixtures of bleb preparations from 2 or more strains, including serotypes P1.15, P1.7,16, and P1.4 (see page 36, lines 15-19). Said vaccine is also disclosed as comprising any or all of the capsular polysaccharides A, C, Y, or W (see page 36,

lines 11-14). Berthet refers to compositions that should be protective against strain CU-385 (page 35, lines 17-30). It is noted that, according to the instant specification, strain CU-385 is deficient in PorA (see page 22, lines 19-22 and page 24, lines 8-11)

Berthet differs from the instant invention in that they do not disclose a composition that comprises blebs from CU-385 in combination with blebs from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand.

Vermont *et al.* disclose an outer membrane vesicle (blebs) vaccine that comprises blebs from a meningococcal strain which has the serosubtype P1.7-2,4 (which is the epidemic serosubtype prevalent in New Zealand) (page 584, column 2, paragraph 1 and page 585, column 1, paragraph 4). As evidenced by Oster (WO 2006/024946, 2006) and Martin *et al.* (Clin. Vacc. Immunol., 13:486-491, 2006), there are different nomenclature systems in use with regard to *Neisseria meningitidis* serosubtypes. According to the different nomenclature systems, serosubtype P1.7-2,4 is the same serosubtype as P1.7b,4.

Baker *et al.* disclose information on the meningococcal disease epidemic in New Zealand. They show that the majority of the strains isolated during the epidemic were B:4:P1.7b,4 (see abstract). Baker *et al.* also suggest that a vaccine that could induce immunity to this strain would be useful in controlling the epidemic (page S18, column 1, paragraph 4).

It would have been obvious to a person of ordinary skill in the art, at the time of invention, to use the bleb preparation from serosubtype P1.7-2,4, as disclosed by Vermont *et al.* in the multivalent bleb vaccine along with a bleb preparation of CU-385 as disclosed by Berthet *et al.* for several reasons. Baker *et al.* state that a vaccine that protects against serosubtype P1.7-2,4 would help to control the New Zealand meningococcus epidemic. In addition, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, the multivalent bleb composition against CU-385 is taught by Berthet *et al.* to be useful in protection against meningococcal disease and the vaccine of Vermont *et al.* is taught to be useful in protection against meningococcal disease. Therefore, it would have been obvious to combine the two vaccines into a single multivalent vaccine. Finally, according to the

Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it would have been obvious to combine elements known in the art by known methods, where in the combination, each element would have performed the same function as it did separately. In this case, vaccines containing blebs from each strain were known in the art, each of these elements would have performed the same function as they would have separately and the results of the combination would have been predictable.

One would have had a reasonable expectation of success because blebs from these strains have been shown to be effective as separate vaccines.

With regard to claims 26 and 28, immunogenicity against heterologous strains and a lack of immune interference are characteristics that are inherently (as can be seen in the instant specifcation) a part of a composition that contains blebs from CU-385 and B:4:P1.7b,4 strains.

Claims 17-19, 26, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Granoff *et al.* (PCT Publication WO 02/09643, 2/7/2002) in view of Vermont *et al.* (Infect. Immun., 70:584-590, 2/2002) and Baker *et al.* (J. Paediatr. Child Health, 37:S13-S19, 2001 for the reasons set forth in the rejection of 1, 6-7, and 16 in the previous office action.

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2. That the claimed combination provides unexpected results, namely, "immunogenicity against heterologous strains" and being "free of immune interference." Applicant argues that combining diverse blebs is discouraged in the prior art because of possible immune interference.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, the combination of prior art references provides a composition containing bleb composition comprising blebs from CU-385 and blebs from strain B:4:P1.7b,4. The specification indicates (and applicant has previously agreed, see remarks filed 11/9/2007) that these strains have the appropriate amounts of PorA. There does not need to be any recognition in the prior art that these strains have the claimed percentages because the fact is that the strains *do* have those claimed percentages.

Regarding argument 2, applicant has not provided any evidence of unexpected results. Applicant has not provided any evidence that the strains would not have separately been immunogenic against heterologous strains and, contrary to applicant's assertion, the art specifically discloses combinations of blebs. Therefore, one would not expect immune interference to be an issue.

As outlined previously, the instant claims are drawn to a multivalent bleb composition comprising a first bleb composition comprising a first bleb preparation deficient in PorA and a second bleb preparation that is not deficient in PorA.

Granoff *et al.* disclose an outer membrane vesicles (bleb) vaccine that comprises a mixture of blebs from genetically diverse strains of *Neisseria meningitidis* as well as a pharmaceutically acceptable excipient (see page 6, lines 23-31 and page 22, lines 5-20). Granoff *et al.* also disclose a bleb vaccine that contains a mixture of blebs from a serogroup C strain as well as a strain with the serogroup P1.4 (see page 7, lines 19-27). Figure 1 discloses a vaccine with the serosubtype B:4:P1.15, that was used in Cuba and Brazil from 1987-1991. Granoff, on page 14, refers to an OMV vaccine prepared by the Finley Institute in Cuba which has been given to millions of children in South America. It is clear from an examination of the art and the instant specification, that CU-385 (commonly referred to as the Cuban strain) is the strain referred to in Granoff on page 14 and in Figure 1. Additionally, Granoff *et al.* disclose that the disclosed mixture vaccine has the advantage of broad spectrum protective immunity (see page 15, lines 10-12).

Granoff *et al.* do not explicitly disclose that the bleb vaccine mixture should contain the strain CU-385 and a B:4:P1.7b,4 strain.

Vermont *et al.* disclose an outer membrane vesicle (blebs) vaccine that comprises blebs from a meningococcal strain which has the serosubtype P1.7-2,4 (which is the epidemic serosubtype prevalent in New Zealand) (page 584, column 2, paragraph 1 and page 585, column 1, paragraph 4). As evidenced by Oster (WO 2006/024946, 2006) and Martin *et al.* (Clin. Vacc. Immunol., 13:486-491, 2006), there are different nomenclature systems in use with regard to *Neisseria meningitidis* serosubtypes. According to the different nomenclature systems, serosubtype P1.7-2,4 is the same serosubtype as P1.7b,4.

Baker *et al.* disclose information on the meningococcal disease epidemic in New Zealand. They show that the majority of the strains isolated during the epidemic were B:4:P1.7b,4 (see abstract). Baker *et al.* also suggest that a vaccine that could induce immunity to this strain would be useful in controlling the epidemic (page S18, column 1, paragraph 4).

It would have been obvious to a person of ordinary skill in the art, at the time of invention, to use the bleb preparation from serosubtype P1.7-2,4, as disclosed by Vermont *et al.* in the multivalent bleb vaccine along with a bleb preparation of CU-385 as disclosed by Granoff *et al.* for several reasons. Baker *et al.* state that a vaccine that protects against serosubtype P1.7-2,4 would help to control the New Zealand meningococcus epidemic. In addition, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, a bleb composition against CU-385 is taught by Granoff *et al.* to be useful in protection against meningococcal disease and the vaccine of Vermont *et al.* is taught to be useful in protection against meningococcal disease. Therefore, it would have been obvious to combine the two vaccines into a single multivalent vaccine. Finally, according to the Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it would have been obvious to combine elements known in the art by known methods, where in the combination, each element would have performed the same function as it did separately. In this case, vaccines containing blebs from each strain were known in the art, each of these elements would have performed the same function as they would have separately and the results of the combination would have been predictable.

One would have had a reasonable expectation of success because the strains have been shown to be effective as separate vaccines.

With regard to claims 26 and 28, immunogenicity against heterologous strains and a lack of immune interference are characteristics that are inherently (as can be seen in the instant specifcation) a part of a composition that contains blebs from CU-385 and B:4:P1.7b,4 strains.

New Claim Rejections

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-22 and 26-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has added claim 17, which recites "derived from a prevalent epidemic strain that is PorA non-deficient 95-105% of PorA, relative to PorA composition of strain H44/76; and a second bleb preparation PorA deficient 0 to 23%, relative to total protein composition of the vesicle." Neither the specification or original claims as filed make reference to 95-105% non-deficiencies or 0-23% deficiencies. Applicant does not point out specific basis for this limitation in the application, and none is apparent. Therefore, this limitation is new matter.

Applicant has added claim 18, which recites "the New Zealand strain (B:4:P1.7-2.4) NZ/228-98." Neither the specification or original claims as filed make reference to strain NZ/228-98. Applicant does not point out specific basis for this limitation in the application, and none is apparent. Therefore, this limitation is new matter.

Applicant has added claim 20, which recites a strain that is "less than 22% in PorA strain different from CU-385." Neither the specification or original claims as filed make reference to such strains. Applicant does not point out specific basis for this limitation in the application, and none is apparent. Therefore, this limitation is new matter.

Applicant has added claim 21, which recites "wherein the first and second blebs maintain the microstructure as proteolyposomes, and are adsorbed into aluminum hydroxide" Neither the specification or original claims as filed make reference to this limitation. Applicant does not point out specific basis for this limitation in the application, and none is apparent. Therefore, this limitation is new matter.

Applicant has added claim 22, which recites "wherein the first and second blebs do not keep the microstructure as original proteolyposomes, but form a microstructure not adsorbed into aluminum hydroxide" Neither the specification or original claims as filed make reference to this limitation. Applicant does not point out specific basis for this limitation in the application, and none is apparent. Therefore, this limitation is new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-22 and 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is rendered vague and indefinite by the phrase "comprising a first bleb preparation derived from a prevalent epidemic strain that is PorA non-deficient 95 to 105% of PorA, relative to PorA composition of strain H44/76; and a second bleb preparation PorA deficient 0 to 23%, relative to total protein composition of the vesicle, and less than 80% relative to the PorA composition of strain H44/76." The language of this claim is confusing. It appears that a strain that is "PorA non-deficient 95 to 105% of PorA" is a strain that has PorA in an amount that is between 95 and 105% of the amount found in H44/76; however the language is awkward and does not convey this. It is also not clear what is meant by "deficient 0 to 23% relative to the total protein composition of the vesicle." It is not clear how the preparation can be deficient relative to itself. It is also not clear whether this means that the 0-23% of the protein is PorA or whether the preparation has 0-23% of the amount of PorA it would normally have or whether it has 0-23% less than it would normally have. In addition, how does this relate to the requirement that there be less than 80% compared to the PorA composition of H44/76?

The term "prevalent" in claim 17 is a relative term which renders the claim indefinite. The term "prevalent" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 21 is rendered vague and indefinite by the phrase "maintain the microstucture as proteolyposomes, and are adsorbed into aluminum hydroxide." The term "adsorb" refers to something adhering to the surface of something else. Therefore, it is not possible to adsorb *into* aluminum hydroxide.

Claim 22 is rendered vague and indefinite by the phrase "do not keep the microstucture as original proteolyposomes, but form a microstructure not adsorbed into aluminum hydroxide." The term "adsorb" refers to something adhering to the surface of something else. Therefore, it is not possible to adsorb *into* aluminum hydroxide. In addition, it is not clear what an "original" proteolyposome is or how a bleb can form the correct microstructure and avoid adsorbing to aluminum hydroxide.

Claims 26 and 27 are rendered vague and indefinite by the phrase "the composition comprises immunogenicity against heterologous strains." As the term "comprise" means "to be made up of", it is not clear how something can "comprise" immunogenicity. Immunogenicity is a characteristic that a composition has, not something is comprises.

Claims 28-29 are rendered vague and indefinite by the phrase "the composition is free of immune interference." Immune interference occurs as a result of an immune response generated by an animal's immune system. Without administration of the composition, there can be no immune interference. Therefore, it is not clear how a composition that is free of immune interference differs from any other composition.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645